

It is important to make a positive diagnosis of diseased cervical lymph glands. The treatment varies with the disease. Some cases of Hodgkin's disease and some of tuberculosis profit by therapeutic operative removal; but with a similar clinical picture in each the operation might not be the same. Likewise, and perhaps more important, if roentgen therapy be employed the dosage which, for example, may help to heal tuberculosis may indeed accelerate the advance of carcinoma, lymphosarcoma and Hodgkin's disease.

Conclusions. 1. Calcification in tuberculous cervical lymph glands is not rare. Although the series here presented is small, the indication is that calcification occurs in 52.5 per cent of such patients over five years of age.

2. A positive diagnosis of tuberculous cervical glands, abscesses and sinuses may be made so frequently by a small plate, studied with the clinical picture, as to render the roentgen ray worth a trial before subjecting the patient to a biopsy.

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THREE CASES OF LEUKEMIA IN ONE FAMILY.*

BY CHARLES W. MCGAVRAN, M.D.,

FORMERLY PROFESSOR OF CLINICAL MEDICINE, COLLEGE OF MEDICINE, OHIO STATE UNIVERSITY; PHYSICIAN TO GRANT HOSPITAL, COLUMBUS, OHIO.

THESE cases are reported not because they present unusual clinical features as leukemia, but because of the interesting facts that three members of one family were affected, and of the most unusual combination, there being one of the myelogenous and two of the lymphatic type.

While there are those who hold that leukemia is of bacterial origin and others that it follows infectious processes of long duration, *i. e.*, tuberculosis, syphilis and malaria, and still others that it is due to a new growth of the blood-forming tissues, yet the fact remains that the etiology of leukemia is unknown. We have no evidence that would prove that heredity is a factor in this disease, although some authors have advanced such a theory. Nor has evidence been produced that would cause one to believe that it is transmitted from man to man.

* Reported to the Columbus Academy of Medicine, November 14, 1921.

Ward¹ has accumulated valuable data as to the familial instance of leukemia, and in his analysis of 1457 cases speaks of Cameron's² cases, which were probably acholuric jaundice, and quoting from Ward as abstracted by Tyce, *Practice of Medicine*: "Ward quotes Obraszow's³ cases, in which a boy who had acute leukemia was nursed by a male nurse who later developed the same type of leukemia; and Bie's⁴ case in which the father of a family died of chronic myeloma, and just before his death a servant girl fell ill of the same disease. Dock's observation⁵ of myeloma in a mother whose daughter later developed the same and whose husband developed splenic anemia one year after his wife's death is also referred to."

In the whole series there are two possible instances of familial cases: Jewett⁶ had under his care a girl, aged seven months, with acute myeloma. He states: "It seems highly probable from the history that a brother and a sister of this child also died of leukemia. The eldest brother at the age of five months developed enlargement of the abdomen and great anemia. He died six months later. The sister at four months developed marked anemia, splenic tumor and emaciation. She died at eight months. Mother and father are alive and well."

Ward remarks that this report is suspicious on the face of it. Leukemia at so early an age very rarely, if ever, manifests itself first by a splenic tumor, but rather by swollen glands, purpura, etc. These were probably cases of Gaucher's disease. Campbell⁷ reported that he knew of a woman under treatment for leukemia whose white cells fell from 400,000 to 5000 after five months' treatment, and adds, 'Her child was under treatment for leukemia at the same time.' There are no further details. Hanesel⁸ reports "acute leukemia in a boy whose uncle was also suffering from the disease. The diagnosis appears to have been quite satisfactorily established, but there is nothing to indicate that it was more than a coincidence."

Ward finds that males are more frequently attacked than females and that each of the three forms has an "age of election." Acute leukemia, occurs more frequently up until the twenty-fifth year and has its highest peak during the first five years; chronic myelogenous leukemia is more prevalent between the ages of

¹ Jordon: The Infective Theory of Acute Leukemia, British Jour. Infect. Dis., January-March, 1917, 14, 10.

² Am. Jour. Med. Sci., 1888, 95, 28.

³ Deutsch. med. Wehnschr., 1800, 91, 1150.

⁴ Ugeskr. f. Laeger, 1910, 74, 1607.

⁵ Am. Jour. Med. Sci., 1904, 127, 563.

⁶ Philadelphia Med. Jour., 1901, 17, 810.

⁷ Lancet, 1912, vol. 1, p. 1473.

⁸ Wien. klin. Wehnschr., 1908, 21, 594.

twenty-five and forty-five years, while chronic lymphatic leukemia more often occurs between the forty-fifth and sixtieth years.

The cause of leukemia being unknown, no opinion will be ventured as to why three male members of the same family were affected with this disease. The author is fully aware that no case report is complete without an autopsy, and particularly that a diagnosis of leukemia is not complete without the pathologic findings of the blood-forming tissues. Two of these cases were under the observation of the author at the same time, and are reported in detail, showing the clinical work that led to the diagnosis.

On July 6, 1920, S. S. L., aged fifty-nine years, a stonemason, complaining of headache, nausea and vomiting, was seen in consultation with Dr. T.

Family History. Father died at eighty-three years of age; mother living, eighty years of age and healthy. There were four brothers—one brother living and healthy at thirty-five; one died at forty of epilepsy; one died at forty of leukemia; one died in childhood, cause unknown. There were five sisters—two are living and well, aged thirty-six and forty respectively; three sisters dead: one died at fifty-eight of tuberculosis, one died at forty-three (cause unknown) and one died at thirty of tuberculosis.

Patient is married (wife is healthy, the mother of four healthy children, and has not miscarried); he has had no previous serious illness. Three years ago he noticed a dry scaly condition on the right side of the face about the size of a nickel. This was diagnosed cancer by Dr. S., who treated it with the roentgen ray every week for a year, but with no improvement. He then consulted Dr. X., who used paste; by this time he had sores on both sides of the face, the lower lobe of the right ear being involved. His face healed promptly after the use of paste, leaving large scars. Since that time until two weeks ago he has been working at his trade. Two weeks ago he began to feel sick, paroxysmal frontal headaches coming specially at night; at about the same time he began to have nausea and vomiting, and has retained little food. His physician found several infected teeth, which have been extracted. His headaches have progressively increased in severity. Today he is delirious.

Physical Examination. "Patient is poorly nourished; muscles of good tone. Hair thin and gray; scalp shows considerable seborrhea. Pupils equal, react promptly to light and distance. Mucous membranes somewhat under color. Patient is confused; seems to see all right but cannot answer questions intelligently. Tongue is coated; teeth chewing-surface poor; gums sore from recent extraction; tonsils cryptic and show evidence of infection; large stellate scars on each side of the face; lobe of the right ear is

deformed; all the superficial glands (submaxillary, cervical, post-cervical, axillary and inguinal) are palpable; they vary in size from an acorn to that of a walnut; they are freely movable and not tender; the radial pulses are equal, regular as to force and frequency, of low tension and easily compressible; blood-pressure, 110/68; the chest and vertebral column are negative; heart and lungs show nothing remarkable; examination of the abdomen is quite unsatisfactory, owing to the extreme muscular rigidity and the mental condition of our patient; he not only does not assist in the examination but moves from side to side, making a satisfactory examination impossible; the abdomen is distended; the area of splenic dullness is increased, but its actual size is not determined; the knee-jerks are preserved.

Discussion. "A very interesting case and one worthy of complete clinical study. Should the glandular involvement be a metastasis from the face, and if the face lesion was a cancer, the prognosis is hopeless. We must not, however, overlook the possibility of lymphatic leukemia or syphilis. Will examine blood, urine and make a Wassermann."

July 7, 1920. Whites, 162,000; lymphocytes, 95; small lymphocytes predominating cell; only moderate number of smudges.

July 7, 1920. Urine: amber; acid; albumin, very slight trace; sugar negative; microscopic: moderate number of red blood cells with occasional pus cell; no casts.

July 8, 1920. Hemoglobin, 80; reds, 4,000,000; whites, 170,000; smears show the same picture as before.

July 8, 1920. Wassermann negative.

July 8, 1920. Diagnosis of lymphatic leukemia is made. Benzol, gr. seven, in capsules t. i. d., and sodium cacodylate, gr. six, intravenously every third day, were recommended.

July 20, 1920. Reds, 4,100,000; whites, 98,500; blood picture shows no change except fewer cells; reds are normal in appearance.

July 31, 1920. Hemoglobin, 80; reds, 3,520,000; whites, 65,000; polynuclears, 2; lymphocytes, 98.

While there was a reduction in the number of white cells following the administration of benzol and arsenic there was no improvement in the patient; he gradually became more toxic and died during the first week of August. Autopsy, although greatly urged, was absolutely refused.

July 8, patient's son came to the office and was told of the diagnosis and the grave prognosis. Among other things the author said: "While your father's blood count is high, it does not compare with that of the patient who just left the room before you entered. While your father has a leukocyte count of 162,000, that man came here four months ago and we found a leukocyte count of over 300,000." "Why, doctor! that man is my father's uncle."

I. C. L., male; married; aged sixty-nine years, farm superintendent, was first seen February 17, 1920.

Complaint. Shortness of breath and precordial pain upon exertion.

Family History. Father died at sixty-three of apoplexy; mother died at seventy-one years of age; there were six brothers: one living and well at eighty; five dead—one died at forty-five of epilepsy; one died at fifty of epilepsy; one died at eight-two years of age; one died at seventy-one of heart disease; one died at seventy-six of heart disease. One sister living and well at seventy-seven; one sister died at sixty-eight, cause unknown.

Present History. Has been a fairly healthy man. Has never had any serious illness. Has lived a life of exposure. Has been subject to frequent colds. For the past fifteen years has had frequent attacks of "catarrh" of the bowels, manifested by abdominal pain and diarrhea. Prior to six years ago had attacks of severe epigastric colicky pain. For the past three years has had shortness of breath and precordial pain upon exertion, gradually becoming more severe. These pains are precordial and radiate up the sternum and down the arms, especially the left. He at times perspires freely, during and after these attacks, and has a feeling of depression and great anxiety. For the past three years has had more or less ringing in the ears. Has no headache. Vision is not disturbed. Appetite is good; eats everything; now masticates well, although until two years ago he was without teeth for twelve years. Bowels are regular; he is a good sleeper; formerly weighed 155 to 160 pounds, but one year ago lost to about 135 pounds. Today weighs 132½ pounds. Kidneys act freely; nocturia one to three times.

Physical Examination. Patient is poorly nourished; muscles of fair tone. Hair gray; scalp in fair condition. Temporal arteries are tortuous; advanced arcus senilis. Pupils equal; react promptly to light and distance. Mucous membranes under color. No marked obstruction to nasal breathing. Tongue is slightly coated; teeth artificial above and below; fauces somewhat injected; tonsils cryptic and show evidence of past inflammation; thyroid negative; the postcervical, axillary, epitrochlear and inguinal glands are distinctly palpable, varying in size from that of a pea to a hickory-nut; they are freely movable and not tender; the larger glands are found in the inguinal region; radial pulses are equal (76), regular as to force and frequency, not of high tension, easily compressible; radial arteries are just palpable; brachials are distinctly palpable and tortuous; blood-pressure, 148/74. Chest is symmetrical; vertebral column negative; decided pulsation in episternal notch; percussion of the chest is negative, cardiac dullness being 11 cm. to the left and 3 cm. to the right of the midsternal line on a level

with the fifth interspace, being 7 cm. at the junction of the third costal cartilage with the sternum. Breath sounds are clear except for many indeterminate rales scattered throughout the chest. Heart tones are clear but metallic. There is a decided cardio-vesicular murmur just over the second left rib. Abdominal examination shows a left inguinal hernia, for which patient is wearing a truss. There is tenderness in the epigastrium. Lower border of the stomach three finger-breadths below the umbilicus—patient in recumbent posture—lower border of liver one finger-breadth below the costal margin; in the midline there is an area of dullness which is probably the liver, extending four finger-breadths below the ensiform appendix. Area of splenic dullness greatly increased. Lower border of spleen distinctly palpable four finger-breadths below the costal margin. Unable to palpate either kidney. The prostate is not specially tender; is hard and nodular.

Discussion. The history of this case is quite typical of coronary sclerosis. It is specially interesting in view of the low blood-pressure. The interesting things brought out in the examination are the involvement of superficial glands together with the enlarged spleen and the general prostatic hypertrophy. Will make the complete clinicals.

February 17, 1920. Hemoglobin, 70; reds, 3,380,000; whites, 330,000; differential; polynuclears, 3; lymphocytes, 95; mononuclears, 2. This is a case of lymphoid leukemia. The predominating cell is the small lymphocyte, although there are a few large and intermediate forms; only a few smudges; the reds show no variation of shape or size. They have a slight washed-out appearance.

February 17, 1920. Urine: specific gravity, 1020; sugar, negative; albumin, slight trace; microscopic: very occasional hyaline cast.

February 18, 1920. Urine, twenty-four hour specimen: 700 cc; specific gravity, 1022; albumin, very faint trace; sugar negative; microscopic: no red blood cells; no casts nor pus cells found. Blood: Whites, 378,000; differential same as reported above. Feces: Formed; dark brown in color; occult blood negative; microscopic: shows no undigested meat fibers; no increase in fat; no parasitic ova.

February 18, 1920. *Fluoroscopic Examination of Chest and Abdomen.* Barium meal shows stomach to be normal in position and contour; definition not good; peristalsis normal; duodenal cap shows no irregularity. There are dense areas beneath the diaphragm on both the right and the left of the stomach. Heart shows nothing remarkable. There is an increase of mediastinal tissue, but this is not marked. In six hours the stomach is empty. Head of the meal in ascending colon; in thirty hours the entire colon is visualized and shows nothing remarkable.

February 19, 1920. *Diagnosis.* Lymphatic leukemia with coronary sclerosis and prostatic hypertrophy. The prognosis is not good.

Patient was advised to rest and was given three injections of arsphenamin in 0.3 gm. doses at intervals of two weeks. At first there seemed to be some improvement; the patient said he felt stronger, and the spleen on March 17 was smaller, being 3 cm. below the costal margin. There was only a slight reduction in the white count. Following the third injection of arsphenamin on March 17 there was a severe reaction and the patient reported on April 14, saying that since he was resting he has had no precordial pain, but that he now felt quite weak. He weighed 131 pounds; spleen was larger than when he first presented himself and a definite increase in size of all superficial glands. His blood showed 400,000 whites, over 98 per cent being lymphocytes, the great majority of which were small.

He was then placed on benzol, gtt. vii, in capsules after each meal, and was sent home with a letter to his family physician, Dr. S., advising that he be given sodium cacodylate, gr. iiij, intravenously, twice a week.

On May 21 the patient returned, saying he felt much stronger. But other than a reduction in the number of the white cells there was no change in his condition; the count showed 144,000 whites; smear shows the percentage of lymphocytes to be about the same; more smudges than in former slides.

On July 7 examination showed no change clinically; blood: hemoglobin, 75 per cent; whites, 198,000; differential unchanged.

On September 1 the patient says he has been working every day, has had no precordial pain and very little shortness of breath; feels much stronger. Blood: Hemoglobin, 85 per cent; whites, 98,000; differential unchanged. The author's remarks on patient's case record on that date were as follows: "The spleen, liver and superficial glands remain unchanged in size. Patient seems stronger, and as long as he improves under benzol and sodium cacodylate will not recommend radium, although should there be an increase in the number of lymphocytes I will at once advise use of radium."

On November 8 the patient returned, saying he felt better, although two weeks before he had a severe attack of neuralgia of the heart, lasting over three hours and requiring a hypodermic of morphin (this was angina). He looks more pale, otherwise no change in his condition. Weight today, 124½ pounds. Blood: Hemoglobin, 75 per cent; reds, 2,500,000; whites, 54,000; smear shows about the same differential, a thin smear giving many smudges; red cells show no irregularities as to shape and size.

It is to be noted that while the patient thinks he is better, the

only change that might be considered as an improvement is the reduction in the number of lymphocytes, in which there has been a notable drop. On the other hand he is more anemic and continues to lose in weight.

A letter from Dr. S., stated that on November 13 the patient became toxic and died on November 20, and that no autopsy had been held.

The son then said, "Five years ago my uncle, W. G. L., died of some blood disease; he was treated by Dr. H. M. Brundage."

Dr. Brundage reports as follows: "I examined my records carefully and can only find the enclosed blood count in the case of Mr. W. G. L. I saw him at the request of Dr. H. The blood count, you will notice, is significant of splenomyelogenous leukemia. I gave him every possible treatment from benzol to the roentgen ray, and even salvarsan was administered. He requested that at his death I should make a postmortem, which, as I remember, did not reveal anything extraordinary outside of a very large spleen."

Clinical report of Dr. Brundage: "Hemoglobin, 78; erythrocytes, 4,616,000; leukocytes, 213,000; polynuclears, 55; small lymphocytes, 4; large lymphocytes, 3; mast cells, 4; neutrophilic myelocytes, 33; eosin, 1. H. M. BRUNDAGE, M.D."

Our great regret is that an autopsy in the case of S. C. L. was absolutely refused. In view of the lack of pathologic evidence these cases are reported at length in order to strengthen the claim of a diagnosis of leukemia.

W. G. L., as reported by Dr. B., and who died of myelogenous leukemia, and S. C. L., who died of lymphatic leukemia, were brothers, and I. C. L., who also died of lymphatic leukemia, was their uncle, being their father's brother.

This family has certainly been "hard hit," for you will observe that in addition to the leukemia there were 3 cases of epilepsy, 2 in the branch I. C. L. and 1 in that of S. S. L. There were also 2 known deaths from tuberculosis in the branch of S. S. L. and 1 doubtful case in the family of I. C. L.

The author does not wish to be understood as trying to strengthen the claim of heredity as a factor in leukemia. He has endeavored to establish the diagnosis of leukemia and to report these cases as a most unusual coincidence. Dr. James H. Warren, associated with the author, has done all the laboratory and fluoroscopic work, and much credit is due him.